

Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986

This medicine is dispensed with a doctor's prescription only

Gavreto 100 mg

Hard capsules

**Composition:**Each capsule contains:
pralsetinib 100 mg

* For information on inactive ingredients and allergens, see section 6 'Additional information'.

Read the entire leaflet carefully before you start using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, consult your doctor or pharmacist.

This medicine has been prescribed to treat your illness. Do not pass it on to others. It may harm them, even if it seems to you that their illness is similar to yours.

1. What is this medicine intended for?

Gavreto is intended for the treatment of certain cancers caused by an abnormal gene called RET (rearranged during transfection):

- In adult patients with metastatic RET fusion-positive non-small cell lung cancer (NSCLC).
- In patients 12 years of age and older with advanced or metastatic RET mutant medullary thyroid cancer (MTC), who require systemic therapy.
- In patients 12 years of age and older with advanced or metastatic RET fusion-positive thyroid cancer, who require systemic therapy and who are radioactive iodine refractory.

Therapeutic group

Tyrosine kinase inhibitors.

How Gavreto works?

In patients whose cancer is due to an altered RET gene, the change in the gene causes the body to make an abnormal RET protein, which can lead to uncontrolled cell growth and cancer. Gavreto blocks the action of abnormal RET proteins and may help to stop or slow lung or thyroid cancer from growing. It may also help to shrink the cancer.

2. Before using this medicine**Do not use this medicine if:**

You are sensitive (allergic) to the active ingredient (pralsetinib) or to any of the other ingredients in this medicine (see section 6 – 'Additional information').

Special warnings about using this medicine**Before treatment with Gavreto, tell your doctor if you:**

- have lung or breathing problems (other than lung cancer).
- have high blood pressure.
- have bleeding problems.
- plan to have surgery. You should stop taking Gavreto at least 5 days before your planned surgery.
- have liver problems.
- are pregnant or plan to become pregnant or if you are an adult man planning on having a child. Treatment with Gavreto can harm your unborn baby or affect fertility. For more information, see the 'Pregnancy, breastfeeding and fertility' section.
- are breastfeeding or plan to breastfeed. For more information, see the 'Pregnancy, breastfeeding and fertility' section.

Children and adolescents

This medicine is not intended for children younger than 12 years of age.

There is no information about the safety and effectiveness of use of this medicine in children younger than 12 years of age.

Tests and follow-up

- Before starting treatment with Gavreto, your doctor will refer you for a test to make sure that the treatment is right for you.
- Women of childbearing age: Your doctor will refer you for a pregnancy test before starting treatment with Gavreto.
- Your doctor will refer you for blood tests before and during treatment with Gavreto to check your liver function.
- You should check your blood pressure regularly, during treatment with Gavreto.

Drug interactions**If you are taking or have recently taken other medicines, including nonprescription medications and dietary supplements tell your doctor or pharmacist.** Gavreto may affect the way other medicines work, and other medicines may affect how Gavreto works. You need to know and keep a list of the medicines you are taking and show it to your doctor and pharmacist when you receive a new medicine.**Using this medicine and food**Take Gavreto on an empty stomach. **Do not** eat for at least 2 hours before and at least 1 hour after taking the medicine.

You should avoid drinking grapefruit juice and eating grapefruit or Seville orange (bitter orange) while on treatment with Gavreto.

Pregnancy, breastfeeding and fertility**Pregnancy**

- Women of childbearing age: Your doctor will refer you for a pregnancy test before starting treatment with Gavreto. The treatment with Gavreto can harm your unborn baby.
- Tell your doctor right away if you become pregnant or if you think you might be pregnant during treatment with Gavreto.

Contraception**For women**

- You should use an effective form of non-hormonal birth control (contraception) during treatment and for **2 weeks** after your final dose of Gavreto.
- Birth control methods that contain hormones (such as birth control pills, injections or transdermal system patches) may not work well during treatment with Gavreto.
- Consult your doctor about the birth control methods that may be right for you during treatment with the medicine.

For menYou should use effective birth control (contraception) during treatment and for **1 week** after taking your final dose of Gavreto.**Breastfeeding**Tell your doctor if you are breastfeeding or plan to breastfeed. It is not known if Gavreto passes into your breast milk. **Do not** breastfeed during treatment and for **1 week** after the final dose of Gavreto.**Fertility**

Gavreto may affect fertility in men and women, which may affect your ability to have children. Consult your doctor if this is relevant for you.

Driving and using machines

Gavreto may make you feel tired. If you feel tired, caution should be exercised.

3. How to use this medicine?

Always use this medicine, Gavreto, according to your doctor's instructions. Check with your doctor or pharmacist if you are not sure about your dose or about how to take this medicine.

Dosage:

Only your doctor will determine your dose and how you should take this medicine.

The recommended dosage is usually: 400 mg (4 capsules of 100 mg) once daily on an empty stomach. **Do not** eat for at least 2 hours before and at least 1 hour after taking the medicine.**Do not exceed the recommended dose.****Do not** change your dose or stop taking Gavreto unless your doctor tells you to.

Your doctor may change your recommended dose, temporarily stop or permanently stop treatment with Gavreto, if you develop side effects as a result of the treatment.

Method of administration:

The capsules should be swallowed whole with a glass of water.

If you have accidentally taken a higher dose or if a child or someone else has accidentally swallowed some medicine, **immediately see a doctor** or go to a hospital emergency room and bring the medicine package with you.**If you forget to take the medicine at the scheduled time**, take it **as soon as** you remember on the same day. Take the next dose at the regular time the next day.**If you vomit after taking the dose, do not** take an extra dose. Take the next dose at the regular time the next day.Adhere to the treatment as recommended by your doctor. Even if your health improves, **do not** stop taking Gavreto without consulting your doctor.**Do not take medicines in the dark! Check the label and dose every time you take medicine. Wear glasses if you need them.****If you have any further questions about using this medicine, consult your doctor or pharmacist.****4. Side effects**

Like with all medicines, using Gavreto may cause side effects in some users. Do not be alarmed by this list of side effects. You may not experience any of them.

Gavreto may cause serious side effects, including:

- **Lung problems:** Gavreto may cause severe or life-threatening inflammation of the lungs that can lead to death. **Contact your doctor right away** if you have any new or worsening symptoms, including:
 - shortness of breath
 - cough
 - fever
- **High blood pressure (hypertension):** High blood pressure is common during treatment with Gavreto and may sometimes be severe. You should check your blood pressure regularly during treatment with Gavreto. **Contact your doctor right away** if you have increased blood pressure readings or if any of the following symptoms appears:
 - confusion
 - headaches
 - shortness of breath
 - dizziness
 - chest pain
- **Liver problems:** Liver problems (increased liver function blood test results) can happen during treatment with Gavreto and may sometimes be serious. Your doctor will refer you for blood tests before and during treatment with Gavreto to check your liver function. **Contact your doctor right away** if any of the following symptoms of liver problems appears:
 - yellowing of your skin or the white part of your eyes (jaundice)
 - dark "tea-colored" urine
 - sleepiness
 - bleeding or bruising
 - loss of appetite
 - nausea or vomiting
 - pain in the upper right side of the stomach
- **Bleeding problems:** Gavreto can cause bleeding which can be serious and cause death. **Contact your doctor right away** if any of the following symptoms of bleeding appears:
 - vomiting blood or if your vomit looks like coffee grounds
 - pink or brown urine
 - red or black stools
 - coughing up blood or blood clots
 - unusual bleeding or bruising of your skin
 - menstrual bleeding that is heavier than normal
 - unusual vaginal bleeding
 - nose bleeds that happen often
 - drowsiness or difficulty being awakened
 - confusion
 - headaches
 - change in speech
- **Tumor lysis syndrome (TLS):** is caused by a fast breakdown of cancer cells. TLS can cause kidney failure and the need for dialysis treatment, an abnormal heartbeat, and may sometimes lead to hospitalization. Your doctor may refer you for blood tests to check if you have TLS. You should stay well hydrated during treatment with Gavreto. **Contact your doctor right away** or get medical help at the hospital emergency room if you develop any of the following symptoms:
 - nausea
 - vomiting
 - weakness
 - swelling
 - shortness of breath
 - muscle cramps
 - seizures

- **Risk of wound healing problems:** Wounds may not heal properly during treatment with Gavreto. **Tell your doctor** if you plan to have any surgery before or during treatment with Gavreto.
 - You should stop taking Gavreto at least 5 days before surgery.
 - Your doctor should tell you when you may start taking Gavreto again after surgery.

Additional side effects:**Most common side effects:**

- constipation
- high blood pressure
- tiredness
- muscle and joint pain
- diarrhea
- decreased white blood cell, red blood cell, and platelet counts
- decreased levels of phosphate in the blood
- decreased levels of calcium in the blood
- decreased levels of salt (sodium) in the blood
- abnormal liver function blood tests

These are not all the possible side effects of Gavreto. **If you experience any side effect, if any side effect gets worse or if you experience a side effect not mentioned in this leaflet, consult your doctor.****Reporting side effects**You can report side effects to the Ministry of Health by following the link 'Reporting Side Effects of Drug Treatment' on the Ministry of Health home page (<http://www.health.gov.il>) which links to an online form for reporting side effects. You can also use this link: <https://sideeffects.health.gov.il>.**5. How to store the medicine?**

Prevent poisoning! To prevent poisoning, keep this, and all other medicines, in a closed place, out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by a doctor.

Do not use the medicine after the expiry date (exp. date) appearing on the package. The expiry date refers to the last day of that month.**Storage conditions:****Do not** store the medicine above 30°C.

Keep the bottle tightly closed in order to protect from moisture.

6. Additional information

In addition to the active ingredient (pralsetinib), the medicine also contains the following inactive ingredients:

Capsule content ingredients: hydroxypropyl methylcellulos, sodium bicarbonate, microcrystalline cellulose (Avice PH102), citric acid anhydrous, pregelatinized starch, magnesium stearate, methanol.

Capsule shell ingredients:

hypromellose, titanium dioxide FD&C Blue #1 (Brilliant Blue FCF), print ink. The white printing ink contains shellac, dehydrated alcohol, isopropyl alcohol, butyl alcohol, propylene glycol, strong ammonia solution, purified water potassium hydroxide, and titanium dioxide is used.

What the medicine looks like and contents of the pack:

Light blue hard capsules with imprint "BLU-667" on one side of the capsule and imprint "100 mg" on the other.

The contents of the pack include a bottle containing capsules and supplied as follows:

- Bottle of 60 capsules.
- Bottle of 90 capsules.
- Bottle of 120 capsules.

* Not all pack sizes might be marketed.

Registration holder's name and address: Roche Pharmaceuticals (Israel) Ltd., 6 Hacharash, POB 6391, Hod Hasharon 4524079, www.roche.co.il.**Manufacturer's name and address:** Hoffmann-La Roche Ltd., CH-4070, Basel, Switzerland.**Approved in March 2022.****Registration number of the medicine in the Ministry of Health's National Drug Registry: 169-37-36872-99**